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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/560,761	04/28/00	PENNA	D 1095R

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EXAMINER	
EINSMANN, J	
ART UNIT	**PAPER NUMBER**
1655	15

DATE MAILED: 10/24/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/560,761	PENNA ET AL.	
	Examiner	Art Unit	
	Juliet C Einsmann	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *1-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4, 8, 11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I in Paper No. 13 is acknowledged. Applicant's election was incomplete because it did not designate a specific sequence for examination as required by the restriction requirement (paper number 12). During a telephone conversation with Steve Callistein on 8/24/01 a provisional election was made with traverse to prosecute the inventions as they relate to SEQ ID NO: 3 and 4. Affirmation of this election must be made by applicant in replying to this Office action. Claims, or portions of claims specifically drawn to other sequences are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Specification

2. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See pages 6, 32, 40, and 44.

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reason(s): The specification discloses sequences that are not properly identified by sequence identifiers. See pages 33, 39, 40, 43, and 55, for example.

In order to comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825), Applicant must submit an amendment directing the insertion of the SEQ ID NOs into the appropriate pages of the specification.

Oath/Declaration

4. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

Information Disclosure Statement

5. The a number of citations listed on the information disclosure statements filed 6/14/00, 6/23/00, and 11/6/00 fail to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the citations of references that are identified by title and "accession numbers" are not complete. These citations do not provide the name of the database whose accession numbers are represented. The content of all references that are properly cited have been considered. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 22-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 22-39 are rejected over the recitation of "phytyl/prenyltransferase protein" and "phytyl/prenyltransferase polynucleotide." The specification does not provide a clear definition which identifies these proteins, and thus it is not possible to determine the meets and bounds of these claims.

Claims 22, 27, and 29 recite method steps of "growing the plant cell." These are unclear because growing the cell will not result in a plant, rather the method step should be directed to regenerating. Claims 22, 27, and 29 further recite "capable of expressing" which is indefinite because it is unclear whether or not the polynucleotide is expressed. The phrase should be changed to which expresses.

In claim 24, the recitation of "vegetables, peppers potatoes, apples" (plural) is inconsistent with "plant" (singular) in line 1 of the claim.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 31-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

It is noted that for these claims a restriction requirement has been applied. The claims have been examined to the extent that they apply to SEQ ID NO: 3.

Claims 31-39 are directed to methods for modulating the level of a phytl/prenyltransferase protein in a plant which comprise transforming a plant cell with a phytl/prenyltransferase polynucleotide and growing the plant cell under conditions to produce a regenerated plant, wherein the phytl/prenyltransferase is selected from polynucleotides having at least 70% sequence identity to SEQ ID NO: 2 and polynucleotides which selectively hybridize to SEQ ID NO: 2. However, with regard to SEQ ID NO: 2, the instant specification only describes a single polynucleotide, that is SEQ ID NO: 2. In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant has possession of a polynucleotide sequence having SEQ ID NO: 2. The subject matter which is claimed is described above.

First, a determination of the level of predictability in the art must be made in that whether the level of skill in the art leads to a predictability of structure; and/or whether teachings in the application or prior art lead to a predictability of structure. The claims are directed methods which utilize phytl/prenylthransferase polynucleotides. With regard to the elected invention, the specification only describes a single protein and a single cDNA encoding that protein and fails to teach or describe any other polynucleotides that are related to SEQ ID NO: 3 within the limitations of the rejected claims. The specification provides no guidance as to how or where the disclosed polynucleotide can be modified yet still maintain the functionality required for the instant methods. The claims also fail to recite other relevant identifying characteristics (physical

and/or chemical and/or functional characteristics coupled with a known or disclosed correlation between function and structure) sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. The claims also fail to recite other relevant identifying characteristics (physical and/or chemical and/or functional characteristics coupled with a known or disclosed correlation between function and structure) sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. Therefore, there is a lack of guidance or teaching regarding structure and function because there is only a single example provided in the specification and because there is no guidance found in the instant specification.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

For the instantly elected claims, only SEQ ID NO: 3 is described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception or written description of phytl/prenyltransferase polynucleotide which has nucleotides modified by addition, insertion, deletion, substitution or inversion with respect to SEQ ID NO: 3 but retaining correlative function in the claimed methods.

10. Claims 22-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, is enabling only for methods for modulating phytyl/prenyltransferase and tocopherols proteins in a plant which comprise transforming the plant with the isolated Synechocystis DNA, SEQ ID NO: 9, does not reasonably provide enablement for methods which utilize other polynucleotides or methods for the modulation of plastoquinone. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

It is noted that with regard to specific sequences, a restriction requirement was set forth, and applicant elected methods which utilize SEQ ID NO: 3. The generic claims have been examined fully, and the claims which specifically recite multiple inventions have been examined insofar as they apply to the elected invention.

These claims are drawn to methods for modulating the level of a phytyl/prenyltransferase protein in a plant, methods for modulating the level of tocopherol in a plant, and methods for modulating the level of plastiquinone in a plant, each of these methods comprising stably tranforming a plant cell with a phytyl/prenyltransferase polynucleotide operably linked to a promoter and growing the plant cell to regenerate a plant which has the appropriate component modified. Claims 23, 38, 30, and 31-39 each recite polynucleotide sequences for use in this method, some reciting specific sequences and some broadening the recitation to include polynucleotides which hybridize to or have homology to the specifically disclosed sequences.

The specification demonstrates one polynucleotide which encodes a polypeptide that demonstrates phenyltransferase activity which results in the modulation of the level of tocopherols in cells. Applicant specifically teaches that the disruption of this gene did not

demonstrate any effect on the activity of plastoquinones, suggesting that there is more than one prenyltransferase active in these cells (p. 33). Applicant teaches the isolation of genes from other plants which have sequence simlarity to the SLR1786 gene (including SEQ ID NO: 3), but applicant does not teach other genes which definitively encode a phytyl/prenyltransferase. The specification does not provide any polynucleotides that have a demonstrated ability to modulate plastoquinones. Furthermore, the specification does not provide any methods which modulate the phytyl/prenyltransferase activity such that a decrease in activity is observed.

Applicant teaches transformed plants with SEQ ID NO: 3 (i.e. the polynucleotide encoding SEQ ID NO: 4) in the positive orientation (see examples pages 55-71). Applicant provides the tocopherol/oil ration in somatic embryos of such plants (pages 60-61). Applicant suggests that the normal range for such ratios would be from 2-5, and that overexpression of the phytyl/prenyltransferase has increased the ratio. However, data is provided from only two controls, one of whose ratios is 7.28 and the other whose ratio is 4.58 (Table 6). Thus, of the two controls, the tocopherol/oil ratio of one is above the "normal" range suggested by applicant, and the other is at the high end of the "normal range." Of the 33 ratios provided in Table 5, 21 of these are within the "normal" range of 2-5. If the normal range is extended to include the ratios between 2 and 7, as observed in the control, then 28 plants are within the normal range. Further it is noted that for the plants which demonstrate high ratios, this appears that it could be as related to low levels of oil as it could be to high levels of tocopherol. The data provided is not sufficient to support the conclusion that SEQ ID NO: 3 is a phytl/prenyltransferase polynucleotide at all, let alone to support a conclusion that the transformation of a plant would modulate the level of a phytl/prenyltransferase protein, a tocopherol, or a plastoquinone.

The state of the art for the isolation of cDNA or genomic clones with a defined functionality is highly unpredictable. Applicant has characterized and isolated a single phytl/prenyltransferase polynucleotide, namely the SLR1736 gene from Synechocystis. Applicant has not demonstrated that any of the other isolated genes have the activity of a phytl/prenyltransferase polynucleotide. It is not clear how the other isolated genes are structurally related to the SLR1736 gene. Hence, it is not at all clear that the disclosed genes, especially SEQ ID NO: 3, are structurally and functionally related to the SLR1736 gene and likewise encode a phytyl/prenyltransferase. Thus, it is not clear that methods utilizing these genes would accomplish the goals set out in the preamble of these claims.

It is noted that the prior art provides methods which comprise transforming plant cells with nucleic acids encoding geranylgeranyl pyrophosphate (GGPP) synthase which is a phytyl/prenyltransferase protein (Ausich *et al.*). These plants are also considered to be within the scope of the claimed invention by virtue of their presence in the prior art.

Moreover, it is noted that the instant claims encompass methods which utilize nucleic acids that are related to SEQ ID NO: 3 based on hybridization or homology. However, Applicant provides no guidance for the regions of the disclosed SLR1736 gene which are essential or sufficient to encode phytyl/prenyltransferase, or for the regions of SEQ ID NO: 3 which are essential or sufficient to encode a phytyl/prenyltransferase. In the absence of such guidance, undue trial and error experimentation would be required to screen the vast number of different polynucleotides with 70% homology to or that would hybridize to SEQ ID NO: 3 to identify those which encode an active phytyl/prenyltransferase, especially in light of the fact that it is not clear from the specification that SEQ ID NO: 3 is a phytyl/prenyltransferase.

The state of the art for modification of gene expression or of phenotypic characteristics in plants by genetic transformation is highly unpredictable and hence significant guidance is required to practice the art without undue experimentation. In genetically modified plants, the introduced transgenes are sometimes not expressed, and they can also result in co-suppression effects. None of these effects are predictable, and the mechanisms of gene silencing are still not fully understood. Moreover, the phenotypic characteristics that will result from expression of a given DNA construct cannot be reliably predicted. In fact, often the expected phenotypic result is not achieved. For example, the instant specification teaches that the blocking of the SLR1736 gene had no effect on plastoquinones when such effects would have been expected.

Given the unpredictability in the art of plant transformation to obtain a specified phenotype, the instant invention is not enabled given the lack of guidance in the specification with regard to what nucleic acids other than SLR1736 can be expected to result in a modulation of phytyl/prenyltransferase levels or tocopherol levels. There has been no showing of a nucleic acid that can modulate plastoquinone levels. In the absence of such guidance, undue trial and error experimentation would be required to screen through the myriad of different DNA constructs and the vast number of transgenic plants to determine how to carry out the methods of the claimed invention. When all of the above is weighed, it is concluded that undue experimentation would be required to practice the invention throughout the full scope of the claims.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 22, 24, and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Ausich *et al.* (US 5684238).

Ausich *et al.* teach a method for modulating the level of geranylgeranyl pyrophosphate (GGPP) synthase (which is a phytyl/prenyltransferase protein) in a plant comprising stably transforming a plant cell with a polynucleotide encoding GGPP operably linked to a promoter in the sense orientation and growing the plant cell under conditions to produce a regenerated plant capable of expressing the polynucleotide for a time sufficient to modulate the level of phytl/prenyltransferase protein in the plant (Example 3, Col. 44-46). Ausich *et al.* teach that the plants produced by this method showed the presence of GGPP synthase, thus the GGPP synthase protein was incerased in the plant (Col. 46, lines 35-40). Furthermore, Ausich *et al.* teach that these methods can be used to transform alfalfa (Col. 6, line 2).

Conclusion

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Einsmann whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the

organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Juliet C. Einsmann
Examiner
Art Unit 1655

October 19, 2001

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600